Cellulose sulfate

Brand Name: Ushercell
Drug Class: Microbicides

Drug Description

Cellulose sulfate, also known as CS, is a high molecular weight carboxymethylcellulose-based polymer. [1]

HIV/AIDS-Related Uses

Cellulose sulfate is currently in Phase III clinical trials to study its effectiveness in preventing the sexual transmission of HIV.[2]

Non-HIV/AIDS-Related Uses

Cellulose sulfate is being tested for effectiveness in prevention of sexually transmitted diseases and for contraceptive use. Preclinical and clinical studies have demonstrated a high level of safety. Laboratory tests reveal the potential of cellulose sulfate to be an effective safeguard against pregnancy and infections from gonorrhea, chlamydia, and herpes simplex virus (HSV)-1 and -2. Placebo-controlled Phase III trials are evaluating its use in the prevention of male-to-female transmission of Neisseria gonorrhoeae and Chlamydia trachomatis.[3] Cellulose sulfate displays direct microbicidal activity against human papillomavirus in vitro.[4]

The contraceptive activity of cellulose sulfate is being studied in ongoing efficacy trials.[5]

In vitro, cellulose sulfate inhibits Gardnerella vaginalis and anaerobes that cause bacterial vaginosis (BV).[6] BV may act as a cofactor in the heterosexual transmission of HIV, so the impact of cellulose sulfate and other vaginal microbicides on BV warrants evaluation.[7] Because cellulose sulfate inhibits BV pathogens, cellulose sulfate may provide contraceptive and antimicrobial activity without increasing a patient's risk of BV.[8]

Pharmacology

Cellulose sulfate gel 6% has been shown to stimulate acrosomal loss, inhibit hyaluronidase, and impede sperm penetration into cervical mucus in vitro.[9] Cellulose sulfate inhibits HIV entry and sperm-egg interaction in vitro, reaching 95% or greater inhibition of sperm binding capacity at a concentration of 1 mg/mL. Cellulose sulfate does not affect sperm motility and is not cytotoxic.[10] [11] Cellulose sulfate inhibits HIV-1 strains with a 50% inhibitory concentration (IC50) of 50 ug/mL. It is especially effective against HSV-1 and -2 at an IC50 of 0.12 to 0.25 ug/mL.[12]

Linear gel spread, as evaluated in a study of 2.5 mL and 3.5 mL gel volumes inserted vaginally, takes place primarily in the first five minutes after gel insertion. Lateral spreading (surface contact) appears to continue after linear spreading slows or stops. Upright patient movement has a greater effect on gel distribution than gel volume does. Using a larger gel volume increases linear spreading but provides less consistent lateral spreading. The greatest linear and lateral spreading have been noted 50 minutes after insertion in women using 3.5 mL of gel who have walked around after insertion. Even under these conditions, women had bare spots in coverage, particularly in the proximal vagina. Thus, the spreading of cellulose sulfate without intercourse did not result in complete vaginal coverage, even at 50 minutes after product insertion.[13]

Vaginal cellulose sulfate tablet inhibition of sperm enzyme and of HIV, HSV, and Chlamydia appears comparable to that of the gel formulation. Cellulose sulfate tablets do not inhibit Lactobacillus in vitro.[14]

In rabbit models, cellulose sulfate 6% gel was active as a contraceptive for at least 18 hours after application and was partially active for at least 24 hours. A gel concentration as low as 0.1% was an effective contraceptive when applied within a half-hour of insemination.[15]

Adverse Events/Toxicity

Cellulose sulfate 6% gel administered vaginally four times daily for 14 days did not differ with respect to epithelial disruption, candidiasis, BV, and acceptability from K-Y jelly placebo.[16] A blinded crossover study of 6% gel was conducted with 2.5 mL and 3.5 mL volumes. Each woman used each gel volume twice; after one application,

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Adverse Events/Toxicity (cont.)

women had restricted upright movement, and after the other, they were allowed to walk around. Excessive leakage was not noted with either volume.[17]

Cellulose sulfate vaginal tablets are not cytotoxic. The gel formulation has shown an acceptable safety profile in macaques.[18] [19]

In a Phase I, two part cohort study of 180 women using cellulose sulfate or K-Y jelly placebo, greater than 80% of women had no problem with either gel, and 65% found the gels easy to use. Fewer women using cellulose sulfate than using K-Y jelly placebo reported genital symptoms in cohort one; new colposcopic findings were detected in only 9% of women using cellulose sulfate, compared to 21% of women using K-Y jelly. In cohort two, fewer women using cellulose sulfate than using K-Y jelly placebo reported genital symptoms; 11% in each group had new colposcopy findings. No differences were statistically significant in any of the groups.[20]

In a survey study of HIV infected women using 6% gel once or twice daily for 14 days, women liked the gel's color, smell, and consistency somewhat to a lot. Overall, 31% of women reported that the gel soiled clothing or bed linens. In women using the gel once daily, 4 out of 7 reported leakage during sex; 4 out of 7 also reported leakage after sex. Many women reported that they would prefer a microbicide that could go unnoticed by a sex partner. Primary issues with the gel were soiling of clothes and leakage of gel during sex.[21]

In a Phase I trial in which men directly applied either cellulose sulfate gel or an active control containing nonoxynol-9 for seven consecutive days, the cellulose sulfate gel was not more irritating than the active control. Symptoms reported by one patient after using cellulose sulfate included slight stinging and mild tingling.[22]

Clinical Trials

For information on clinical trials that involve Cellulose sulfate, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Cellulose sulfate AND HIV Infections.

Dosing Information

Mode of Delivery: Intravaginal.[23]

Dosage Form: Cellulose sulfate 6% vaginal gel in a 3.5 mL prefilled applicator for insertion prior to sexual intercourse.[24] [25]

Cellulose sulfate 200 mg vaginal tablets containing excipients generally regarded as safe (GRAS). Tablets disintegrate in less than 30 seconds in 10 mL of fluid to form a smooth, homogenous, viscous, and bioadhesive dispersion.[26]

Cellulose sulfate 6% vaginal gel has been tested in women up to four times daily for up to 14 consecutive days.[27] [28] [29]

Cellulose sulfate 0.1% vaginal gel has been tested for contraceptive use.[30]

Because the optimal applied volume of gel is not known, volumes ranging from 2.5 mL to 5 mL have been tested.[31]

Chemistry

CAS Name: Cellulose, hydrogen sulfate[32]

CAS Number: 9032-43-3[33]

Physical Description: Cellulose sulfate is a thick and odorless gel with a slightly hazy, light brown tint.[34]

Stability: Vaginal tablets stored in accelerated stability conditions recommended by the International Council on Harmonization (ICH) for Zone IV countries were stable for a period of three months.[35]

Other Names

Sodium cellulose sulphate[36]

Sodium cellulose sulfate[37]

CS[38]

Cellulose sulphate[39]

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Further Reading

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For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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